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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,099	11/21/2001	Scott A. Lesley	P0012US20	1291

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,099	LESLEY ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9 and 11-76* is/are pending in the application.

4a) Of the above claim(s) *34-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-6,8,9 and 11-33* is/are rejected.

7)☒ Claim(s) *3,7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is a reply to the "Response to Office Action" of 6 October 2003 (hereinafter, 6 October Paper) filed in response to the Non-Final Office Action mailed 18 June 2003 (hereinafter, 18 June Office Action). Claims 34-76 were withdrawn from consideration and claims 1-33 were considered in the 18 June Office Action. Claim 10 was canceled and claim 1 was amended in the 6 October Paper. Claims 1-9 and 11-76 are pending and claims 1-9 and 11-33 are presently under consideration.

Election/Restrictions

This application contains claims 34-76 and host cells comprising solubility responsive promoters selected from SEQ ID NO: 1-21 and 24-43 drawn to an invention nonelected with traverse. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

It was noted in the 18 June Office Action that copending application 09/991,499 and 10/127,078 appear to contain closely related subject matter suggesting that the claims of 10/237,060 and this application may recite the same or overlapping Inventions. It was further stated that, if, upon availability of the above application to the Examiner, it is determined that there are conflicting claims between 09/991,499 or 10/127,078 and the instant application, double patenting will not be considered as new ground(s) of rejection.

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of copending Application No. 10/127,078 and claim 10 of copending Application No. 09/991,499. Although the conflicting claims are not identical, they are not patentably distinct. The instant claim is directed to a host cell comprising a solubility responsive promoter linked to a reporter gene and a polynucleotide encoding a target polypeptide that is heterologous to the host cell. The conflicting claims are directed to a host cell comprising a solubility responsive promoter linked to a reporter gene and a polynucleotide encoding a target polypeptide wherein the polynucleotide that encodes the polypeptide is heterologous to the host cell. Given that a polypeptide encoded by a polynucleotide that is heterologous to a host cell would also be heterologous to a host cell, the limitations of the instant claim 1 would be obvious to one of ordinary skill in the art from the

limitations of claim 3 of copending Application No. 10/127,078 and claim 10 of copending Application No. 09/991,499.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Amendment

Rejection of claim 10 is rendered moot by cancellation of the claim.

Claim Rejections - 35 USC § 112

Claims 1, 2, 4-6, 8, 9 and 11-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record and herein below in the response to arguments.

Claim Rejections - 35 USC § 102

Rejection of claims 1, 5, 8, 11, 14-18, 22-25 and 28 under 35 U.S.C. 102(b) as being anticipated by Farr U.S. Patent No. 5,589,337 is withdrawn.

Claim Rejections - 35 USC § 103

Rejection of claims 1-8, 11, 14-18, 22-25 and 28 under 35 U.S.C. 103(a) as being unpatentable over Farr in view of Allen *et al.* (1992) *J. Bacteriol.* 174:6938-6947 is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

Claims 1, 2, 4-6, 8, 9 and 11-33 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action contends that the skilled artisan would not have viewed the teachings of the specification as sufficient to show that the applicant was in possession of the claimed invention commensurate to its scope because it does not provide adequate written description for the broad class of solubility responsive promoters.

In response to the rejection of record, Applicant asserts that he instant rejection appears to have been made on an incorrect assumption that the subject invention is directed to protein solubility responsive promoters per se. Applicant urges that the claimed invention is directed to host cells harboring a solubility reporter construct and an exogenous polypeptide-encoding polynucleotide, and to methods of using such host cell to determine solubility of the target polypeptide.

These arguments have been fully considered but are not found persuasive because, as pointed out in the previous Office Action, the solubility responsive promoter is a critical functional element of the claimed host cell. Applicant argues that patentability of the claimed invention is predicated on the novel concept of employing a protein solubility reporter construct to determine solubility of a polypeptide encoded by an exogenous polynucleotide in the host cell. However, the claims are not directed to a concept but to a specific product and method of using a product in which the solubility responsive promoter is the critical operative component. In an unpredictable art, description of a method in broad conceptual terms does not adequately describe all products made by or used in the method, and adequate description of a method

requires adequate description of those elements used in the method that are critical to its function. It should be noted that none of the solubility promoters disclosed in the application would be operative in eukaryotic cells and probably would not function in many, if not most, prokaryotic cells. In spite of this, Applicant is claiming to be in possession of any eukaryotic or prokaryotic host cell comprising a solubility reporter nucleic acid wherein expression of a target polypeptide in an insoluble form causes a change in expression of a reporter gene because, in essence, the specification discloses how one might use such a cell. On the contrary, naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Applicant urges, "[t]he law of written description does not require Applicants to disclose representative members of all possible species for these features of the claimed invention. Otherwise, in order to satisfy the written description requirement, Applicants will also have to disclose representative members from all possible species for the other elements recited in the claims, e.g., the host cell, the target polypeptide, or the reporter gene. Such a requirement would surely represent a novel, unreasonable and unwarranted extrapolation of the law" (page 15). This argument is not deemed persuasive because the written description requirement does in fact require disclosure of a representative number of species for those aspects that are not conventional in the art. In contrast to the host cell, reporter gene, or target polypeptide, the solubility reporter gene is not conventional in the art. The solubility responsive promoter must have the properties of being induced or repressed in a cell in response to an increased concentration of insoluble protein in the cytoplasm. Further, given that the host cell can be any host cell, possession of the full scope of host cells encompassed by the claim would require

possession of a solubility responsive promoter capable of being induced or repressed in a cell in response to an increased concentration of insoluble protein in the cytoplasm regardless of the particular host cell in which the promoter is comprised. Clearly, such a promoter is not conventional in the art and the skilled artisan would have no idea what the relevant identifying characteristics of such a promoter would be. Therefore, the skilled artisan would not recognize that Applicant was in possession of the full scope of the claimed host cells and methods of using the host cells at the time of filing.

Applicant next argues that the instant claims are analogous to a novel process for manufacturing furniture with wood. However, this analogy fails because various types of wood and furniture are conventional in the art while solubility responsive promoters having the characteristics of the promoter comprised within and critical for the function of the claimed host cell are not conventional in the art. Applicant's analogy oversimplifies the issues at hand. Biological systems are not like furniture because one of ordinary skill in the art cannot readily predict the structural characteristics that will provide the recited function. One of ordinary skill in cabinet making knows that if one supports a platform with four properly positioned posts it will function as a chair. What is more, one would know that it has that function regardless of what the platform and posts are made of, or who might be sitting on the chair. But what if the making of a functional chair required the exact positioning of thousands of legs, and what if the correct positioning was dependent upon the particular characteristics of the person that is to sit on the chair? What if, by empirical experimentation, one of skill in the art discovered a configuration of several thousand pillars that would function as a chair only for persons having a particular height, weight, hair color, eye color and shoe size? Would a description of this chair

adequately describe all chairs even though it would not function as a chair for the vast majority of people? Would a method of sitting on a chair be adequately described even if most people would fall to the floor if they tried to sit on the only known structure having the functional characteristics of a chair? It would seem not.

Applicant urges that the specification has disclosed in great detail how to use a solubility responsive gene promoter, that the specification discloses that the protein solubility responsive promoter can be a prokaryotic or a eukaryotic promoter, that there are many eukaryotic heat shock and other stress-induced genes that are well known in the art and that the specification teaches how to identify potential solubility responsive promoters from various eukaryotic cells. These arguments are not persuasive because, as stated in the previous Office Action, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself. It is not sufficient to define DNA solely by its principal biological property, i.e., it has the function of a solubility responsive promoter, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property" (page 7). Applicant is again reminded that the elected claims are directed to a product and method of using a product having unpredictable structural characteristics. A description of how one might use, or where one might go search for a product having the recited functional characteristics does not adequately describe the invention.

Applicant states, "[i]n addition to the protein solubility responsive promoters that can be employed in the claimed invention, the specification also provides detailed description of solubility reporter gene constructs (e.g., pages 19-22) and suitable host cells (e.g., pages 18-19).

The specification further discloses methods for delivering the reporter construct into the host cell (e.g., page 22, lines 10-16), methods for detecting and quantitating reporter expression (e.g., page 20), and methods for measuring the amount of soluble or insoluble target protein (e.g., page 24, lines 6-27)." These aspects of the invention are not at issue. The rejection is based on the failure of the specification to fully describe the generic solubility responsive promoter, which is critical to the function of the claimed invention.

Applicant points out the reduction to practice of the claimed invention demonstrated by the various examples provided in the specification. However, the reduction to practice is limited to a bacterial host cell. As pointed out previously, the solubility responsive promoters used in the working examples would not function in the vast majority of host cells encompassed by the claims. Thus the working example is not representative of the vast majority of the claimed genus.

Applicant acknowledges that if the invention is directed to protein solubility responsive genes or promoters *per se*, one might reasonably cast doubt as to whether there is adequate written description of the claimed invention to the extent that it is directed to all possible promoter solubility responsive promoters. However, Applicant alleges that there is not doubt the present inventors indeed had possession of host cells harboring a solubility reporter construct. Applicant urges that while not all host cells or protein solubility responsive promoters have been described in the specification, they are either well known can be easily identified; that although different host cells and solubility responsive promoters may vary tremendously in terms of their biological and biochemical properties, the exact nature of these materials is not essential to practicing the claimed invention.

These arguments are not deemed persuasive. Applicant appears to acknowledge that there is reasonable doubt that the genus of solubility responsive promoters is adequately described, yet maintains that claims to a host cell and method wherein the solubility responsive promoter is the single critical functional element are fully described. The instant specification does not provide a single specific example of a promoter that could be used in the construction of a eukaryotic host cell wherein expression of a target polypeptide in an insoluble form causes a change in expression of a reporter gene. In spite of this, Applicant claims to be in possession of any eukaryotic or prokaryotic cell having these functional characteristics because the specification teaches how to use such a host cell or how to search for a promoter that could be used to make the host cell. However, given the tremendous breadth and diversity of the claimed subject matter, the absolute requirement that one be in possession of the protein solubility responsive promoter in order to make or use the claimed invention, and the failure of the specification and art to provide an actual description of a solubility responsive promoter that could be used to make the vast majority of the claimed host cells, one of ordinary skill in the art would not have recognized that Applicant was in possession of the full scope of the claimed subject matter at the time of filing.

Applicant's arguments have been fully considered but are not deemed persuasive either individually or as a whole. Therefore, the claims stand rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description for the claimed subject matter.

Allowable Subject Matter

Claims 3 and 7 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 703-305-4448. The examiner can normally be reached on Monday through Friday 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Please note: Art Unit 1636 will be moving to the new USPTO facilities on 14 January 2004. After that date, Examiner Sullivan can be reached at 571-272-0779 and Examiner Yucel can be reached at 571-272-0781.

DMS

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER